A PERIENDOTHELIOMA OF THE DURA MATER INVOLVING THE CRANIAL NERVES.[1]

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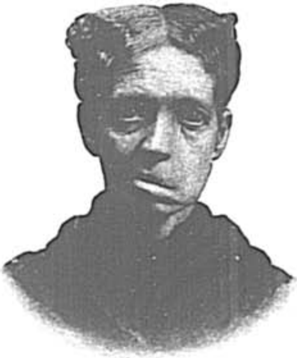
Report of Dr. Brower.

Mrs. W., aged forty-seven years, was brought to my clinic, October, 1890, by Dr. Annetta S. Dobbins, with the following history: She was admitted to the Woman's and Children's Hospital, May 28, 1882, complaining of a sense of weariness on the slightest exertion, of an intense earache in the left ear, a severe headache, and pain and swelling of the left side of the face. There was a slight trace of albumin in the urine, and a slight aortic regurgitant murmur. She had had three living children and six miscarriages. Under treatment she improved, and was discharged June 29, 1882. On January 6, 1883, she returned to the dispensary of the hospital, on account of a distressing and peculiar cough. The following June she again returned to the hospital with a transitory attack of left hemiparesis, the sensory impairment

Fig. 1.



The patient as she appeared at my clinic, December, 1897.

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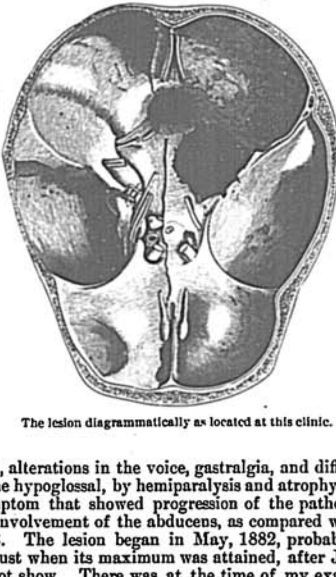
[1] Presented at the meeting of the Chicago Pathological Society, January 14, 1901, with specimens.

being more marked than the motor, and the cough of the preceding winter more harassing. A month later she had another miscarriage, in which there was an unusual loss of blood. She was again taken to the hospital, and there the facial paralysis was detected, and on examination all the cranial nerves below the fourth except the abducens were found to be involved. On my examination I found paralysis of the motor and sensory branches of the trigeminus on the left side; of the abducens manifested by strabismus, diplopia, and dizziness; of the facial, a complete facial paralysis, the muscles showing the reaction of degeneration; the auditory, with a complete loss of hearing; of the glossopharyngeal, shown by a posterior ageusia; of the pneumogastric and spinal accessory, shown by the cough, disturbed respiration and heart's action, alterations in the voice, gastralgia, and difficulty in swallowing; of the hypoglossal, by hemiparalysis and atrophy of the tongue. The only symptom that showed progression of the pathological condition was the involvement of the abducens, as compared with the record made in 1883. The lesion began in May, 1882, probably slowly progressed, and just when its maximum was attained, after July, 1883, the record does not show. There was at the time of my examination also atrophy of the left sternocleidomastoideus and of the upper part of the trapezius muscles. Albumin was still present in the urine, and a slight aortic regurgitant murmur, and the arteries showed marked sclerosis. She had had at this time in all twelve miscarriages. The family history was negative; the mother was still living, and the father had died a few months before of cardiac disease.

FIG. 2.



The lesion diagrammatically as located at this clinic.

We made the diagnosis of meningeal tumor, because the symptoms continued to be unilateral until the end. Nuclear lesions are almost invariably bilateral, or soon become so, and, moreover, there was no progression upward or downward. I excluded an amyotrophic lateral sclerosis and progressive bulbar paralysis.

There were at no time in the case any pressure symptoms manifest. Repeated examinations were made of the optic fundus, and nothing abnormal found. Interesting features of the case are, first, its long period of quiescence; beginning with 1890 till the time of her death the case was shown every year at my clinic, and the symptoms showed no progression. The growth of the tumor, also, must have been slow. The next interesting fact is the absence of pressure symptoms, and the third interesting one, and the very important one, is the fact that the pathological study of the tumor excludes syphilis in its pathogenesis, and makes it a benign tumor of the perithelial variety. We supposed it was syphilitic, because of her numerous miscarriages, none of which were the product of violence, and because of the marked arterial degeneration which she had, and because of glandular enlargements, and because of the benefit derived from the use of antisyphilitic remedies. She was probably a syphilitic patient with a non-syphilitic brain tumor, and this fact should make us more cautious in referring the genesis of nervous symptoms to syphilis in syphilitic patients.

The patient died of angina pectoris.

Pathological Report by Dr. Wells.[1]

Autopsy was performed twenty-six hours after death by Dr. S. M. White and myself. The body was that of a slenderly built, poorly nourished woman. It was noticeable that the mouth was drawn to the right and that the left cheek was thinner through its substance than the right. The chief findings in the body were the following:

1. A marked general arterio-sclerosis, seen especially in the larger branches, such as the splenic and coronaries, which were calcified into unyielding, tortuous tubes.
2. Calcification of the aortic valves, without incompetence to the water test or stenosis.
3. Hypertrophy of the left ventricle.
4. Advanced chronic interstitial nephritis.
5. A neoplasm of the dura, extending into the petrous portion of the left temporal bone.
6. Left hemiatrophy of the facial muscles and of the tongue.

Nowhere in the body could lesions characteristic of syphilis be found, although on account of the history of the case and the provisional diagnosis they were looked for most carefully. The extensive arterio-sclerosis and the calcification of the aortic valves could have been syphilitic, but were not necessarily so.

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[1] From the Laboratory of Pathology, Rush Medical College.

On opening the cranial cavity nothing abnormal was found over the surface covered by the calvarium. The left inferior posterior fossa, however, was found to be occupied by a mass binding the dura firmly to the skull, less so to the brain. The dura, brain, and tumor mass were removed *in toto* by cutting the growth out of the petrous bone. It was found that this bone had been invaded anteriorly as far as the foramen lacerum medium and along the superior border of the petrous portion of the temporal, and posteriorly to the margin of the foramen magnum, although not into it. The mastoid process had disappeared. This location and extent, it will be noticed, exactly agrees with the provisional location determined from the clinical findings as shown in Fig. 2.

On complete removal the tumor was found to consist of a dense tissue, resembling fibrous tissue in most places, although toward the median line were several softer, reddish, nodular masses. The greatest length of the tumor is antero-posteriorly, this diameter measuring 6.5 cm.; transversely it measures 4 cm., and the same in thickness. More of the growth is external than internal to the dura mater, which seems to bisect it. Its superior surface is in contact with the inferior surface of the left cerebellar hemisphere and the posterior portion of the temporo-sphenoidal lobe, but it is not adherent to the brain nor to the pia mater. It is held attached to the brain by the vessels and nerves entering its substance. On the internal surface it is in contact with the pons and the anterior half of the medulla. It is quite plain why the paralysis involved just the nerves it did—the fifth to the twelfth inclusive. The fourth, rising from its deep nucleus in the floor of the aqueduct of Sylvius, and emerging in front of the pons from the outer side of the crus, would escape any direct pressure from the growth. On the other hand, the fifth, emerging from the lateral aspect of the pons, would be pressed upon at this point, and also as far forward as the Gasserian ganglion. Similarly all the other nerves behind the fifth would be destroyed. Unfortunately, during the removal of the brain the nerves behind the third were torn from the brain at their roots, so that the changes in them cannot be studied.

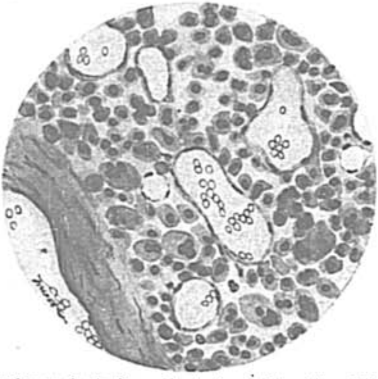
Connecting the growth to the brain are the anterior and inferior cerebellar arteries and small branches from the left vertebral. Anteriorly the internal carotid enters and courses backward and internally in its substance to emerge near the inner anterior angle. Its walls are much thickened (sclerotic), but not invaded by the tumor tissue, in which it lies in a distinct sheath, nor does the lumen seem lessened by pressure.

The left lobe of the cerebellum is atrophied so that only the posterior half remains, and this remnant is pushed to the right so that its middle line corresponds to the right edge of the medulla, the left tonsillar lobe lying over the lower end of the fourth ventricle. The left temporo-sphenoidal lobe is flattened so that it is about two-thirds the size of the right; this is the result of the lessening in size of the convolutions rather than to a disappearance of them. The medulla is pushed slightly to the right, and the left olive seems smaller than its fellow. The left half of the pons is greatly atrophied, being but 7 to 10 mm. in thickness, while the right is 12 to 18 mm. thick. This atrophy involves the entire left side of the pons. A special study of the changes in the central nervous system will be reported subsequently.

On cross-section the tumor is found to be exceedingly vascular, in some portions almost spongy with bloodvessels. The peripheral portions are less vascular than the central and more fleshy, the centre being rather fibrous. In consistency it is firm, but quite elastic. Many minute granules of calcified material are present near the centre, but absent in the periphery, barely visible to the naked eye as clear, sand-like particles. Except where torn in removal from the bone the growth is distinctly surrounded by a thin, fibrous capsule. The dura loses its identity in the tumor, no traces of it being visible on the cut surface.

Microscopically the different portions of the tumor vary slightly in structure, but are made up in varying portions of bloodvessels, which are always numerous, stroma, and tumor cells. For the most part the vessels are the prominent feature, for in some sections they are so numerous as to resemble an angioma. This is especially true of the peripheral portions of the growth. In the centre the vessels are larger, generally surrounded by considerable connective tissue, and but few of the small vessels are to be seen.

FIG. 3.

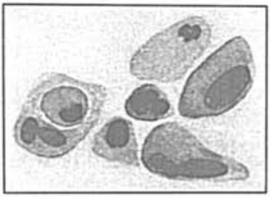


Section of tumor, showing its vascular structure and the relation of the tumor cells and vessels.

The larger vessels have walls consisting of an internal layer of endothelium and a series of laminæ of connective tissue surrounding it, with apparently no muscular tissue. They differ from the smaller vessels solely in size and in the amount of connective tissue in their walls. The very smallest capillaries always possess these two layers, an internal lining of endothelium and a layer of connective tissue, which may, however, consist of but little more than a basement membrane supporting the endothelium. No changes were seen in the endothelium, which is identical with that of adult vessels; nowhere is it found proliferating. In proportion to the thickness of their walls the lumen of the smaller vessels is large, so that they resemble the vessels of granulation tissue (Fig. 3).

In the peripheral and most vascular portions the numerous vessels are entirely surrounded by the tumor cells, which fill all the space between them in such a way that it might be said either that the tumor cells form the stroma for the vessels of an angioma or that the vessels form the stroma for the cells In these parts the bulk of the tissue is about equally vessels and cells. Between the cells there is no stroma. The cells are of several types (Fig. 4). For the most part they have a deeply staining spherical nucleus, often eccentrically placed. The protoplasm is quite abundant, and its shape depends entirely upon the surroundings. Sometimes it is symmetrically disposed, and we find a large round or polygonal cell with a relatively small nucleus duplicating a large mononuclear leücocyte or a flat endothelial cell. Again, the protoplasm may be pressed out so that the cell tapers, shaped like a tadpole, with the nucleus at the head. The margin of the cells is always clear, and usually we find a space separating them. Many of the cells are multinuclear, even those that are quite small sometimes having two nuclei. The large multinuclear cells are of various types. The commonest form is about the size of the ordinary endothelial cell when viewed on the flat surface, and has from four to eight nuclei, which are usually near one end. Occasionally the nuclei are peripherally arranged, resembling a small, tuberculous giant-cell, but this form is exceptional. The shape varies with the surroundings, but is generally polygonal. When the cells are cut across the nuclei are seen to lie in a mass upon each other, and it is demonstrated that these large cells are usually flat and of the general structure of endothelial cells. Cells are also seen that seem to contain small cells within their protoplasm, resembling phagocytic endothelial cells as seen in lymph glands in the acute infectious diseases. Another type of the large cell has what at first sight appears to be a giant nucleus, but which is in reality a mass of nuclei, superimposed and apparently partly coalesced. A few cells, however, have a single enormous nucleus, staining intensely, very granular or ragged in structure. Probably such large cells as have just been described might be called mononuclear and multinuclear giant cells. Karyomitosis was not observed in a single instance.

FIG. 4.



Different types of cells.

As to the arrangement of the component parts of the tumor, the unit seems to be a bloodvessel surrounded by a mass of tumor cells. Whether this vessel is very thinned wall and with a large lumen, as is usually the case, or is covered by a thick mass of fibrous tissue, does not seem to influence the arrangement. Just outside of its connective tissue walls are always to be found the tumor cells, which are in contact with the connective tissue, but not united to or entangled in it, a distinct line of demarcation being present between the two structures as clearly as between an epithelial structure and its basement membrane. Between one vessel and its nearest neighbor lie only the cells, without any fibrous structure whatever. In other words, as before mentioned, the tumor cells may be considered as stroma holding the bloodvessels in position or the bloodvessels may be considered the stroma of the tumor. The only connective tissue demonstrable by Van Gieson's method is that about the walls of the vessels, or processes which occasionally branch from the larger vessels and the capsule, which run but short distances and seem to connect with vessels.

In the gross specimen calcified spicules were found. It is seen microscopically that these are not simple granules of calcium salts deposited in degenerated tisues, but true bone. None of them is large, and all are surrounded by a fibrous capsule. Within the calcified tissue the bone corpuscles with their branching projections into the canaliculi are plainly seen, most numerous just beneath the investing fibrous membrane. No other evidences of degeneration are found.

Just where to place this tumor as to classification is a matter of much interest. Primarily it must be considered a benign growth, as shown by its clinical history and its gross anatomy. It is evidently a vascular tumor, differing from the simple angiomas in possessing an intervascular matrix of cells of endothelial type. Borrmann[1] has classified the tumors of vascular origin in a way that seems especially clear and satisfactory, as follows:

1. ANGIOMA.

Hæmangioma.	Lymphangioma

2. ENDOTHELIOMA.

Hæm(angio)-endothelioma. (No capillaries.)	Lymph(angio)-endothelioma. (The common endothelioma of the literature.)
Consists of vessels with a characteristic wall, which are filled with proliferated endothelium. Growth apparently not from new formation of vessels, but only through proliferation of the vessel-endothelium.	Consisting of cell-cylinders and cell-columns which lie in the lymph spaces. Growth by progression of the proliferating endothelium of the tissue spaces and lymph vessels along the course of the latter.

Capillary-endothelioma.

Consists of new-formed (tumor) capillaries, which arise from proliferated capillary-endothelium. The capillaries become filled finally by growing endothelium. Grows by newly formed capillaries which are protruded as fine tubes or cylinders.

3. PERITHELIOMA AND PERIENDOTHELIOMA.

Perithelioma.

Development unknown. Consists chiefly of many vessels with many-layered, superimposed, radially arranged cells, which lie perpendicularly on the outer wall of the vessels.

Peri-endothelioma.

Development unknown. Consists chiefly of many vessels with many-layered, superimposed cells, arranged concentrically about the outer wall of the vessel, with their long axis in the direction of the vessels.

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[1] Borrmann. Virchow's Archiv, 1899, Bd. clvii. p. 297.

In the tumor under discussion it is found that the cellular portion always surrounds vessels, and is always the only structure between any two adjacent vessels. These cells do not seem to be in any way related to the endothelium lining the vessels, being always separated from them by a wall of connective tissue. Evidently they form for the vessels of the tumor a perithelial structure, for they lie outside of every vessel and form the tissue separating the vessels. As a perithelioma we recognize under Borrmann's classification a tumor whose cells are of the spindle-cell sarcoma type, arranged more or less radiating from the vessel they surround. Here, however, the cells are not of the ordinary sarcoma type, but are flat cells which, with the exception of being multinuclear in many instances, resemble typical endothelial cells, even to the extent of sometimes acting as phagocytes for other smaller cells. The only cells in the adventitia from which such a tumor can arise are in the lymphatic sheath surrounding the vessel. Such tumors Borrmann calls periendothelioma, which is perhaps as exact and descriptive a name as any for such a growth. He states that in such tumors the cells are arranged parallel to the vessel wall, in contradistinction to the radial arrangement of the perithelioma or angiosarcoma. In this dural tumor no definite arrangement of the cells is seen; they seem to simply fill the spaces between vessels, and may be found cut in every direction in relation to the section of the vessel they surround.

Endothelioma of the dura mater is generally a benign tumor, less often malignant than when arising in the pleura and peritoneum, and still less so than endothelial tumors of the ovary and testicle.[1] It is especially the case that psammomas or sand-tumors are benign, and this tumor macroscopically might be classed as psammoma, although the number of calcific granules was smaller than usually are found in such growths. The calcareous infiltration in psammoma, however, is never an ossification, but simply a deposit in degenerated connective tissue (Sailer). Virchow[2] has recently defined his original use of the term "psammoma," and states vigorously that it does not include the endothelial tumors.

Giant cells have been occasionally recognized in endothelial tumors. Brosch[3] and Glockner[4] have both studied them. The latter describes both the mononuclear and multinuclear types seen in this case, and found them in four of sixteen endotheliomas of the pleura or peritoneum. He considers their origin to be the same as that of the small cells about them—that is, from the endothelium—and due to rapid division of the nucleus without division of the protoplasm. Others, he

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[1] For a complete and excellent discussion of the subject of endothelial tumors, see article by Sailer in the Contributions from the Pepper Laboratory, Philadelphia, 1900, p. 416.

[2] Virchow's Archiv, 1900, Bd. clx. p. 32.

[3] Ibid., 1896, Bd. cxliv. p. 289.

[4] Ziegler's Beitrage, 1899, Bd. xxvi. p. 73.

thinks, may form from direct segmentation and fragmentation of nuclei. The large uninuclear giant cells are probably the result of abnormal karyokinesis, and possibly also produced by fusion of a number of single nuclei. Sailer considers that in his case the multinuclear giant cells are apparently aggregations of cells, and many features of my own specimens suggest such an origin. In justice it must be said, however, that identical appearances would be produced by a division of the giant cells into smaller cells, and as a possible confirmation of this view is the much greater frequency of giant cells in the newest parts of the growth. Glockner considers it possible that the giant cells may undergo such a splitting up into small cells. One other source for the giant cells in this case must also be considered. The dura serves not only as a serous membrane, but as a periosteum for the skull, and any tumor arising from periosteum is, of course, especially likely to contain giant cells. In this connection may be recalled the ossified granules previously described. However, giant cells have also been found in endotheliomas not connected with bone—*e. g.*, the pleura, peritoneum, pulmonary vein.

In conclusion, this tumor may be stated to represent a benign growth of the dura mater, derived from the endothelium of the lymphatics of the perithelial layers of the bloodvessels, the periendothelioma of Borrmann. As special structural features may be mentioned the presence of many uninuclear and multinuclear giant cells and spicules of true bone.

GONORRHŒAL MYOSITIS.[1]

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The earliest reports of the biological history of the gonococcus accorded it merely the rôle of a local parasite whose habitat in the genito-urinary tract was determined by its predilection for the epithelium here found, though long before the day of the specific gonococcus, clinical experience had taught us of the contemporaneous existence of joint inflammations during the gonorrhœa; yet not till the finding of the gonococcus in the joint secretions by Kammerer, Hartley, and others was the presumed barrier to its growth in tissues other than epithelial broken down. From that time on we have had overwhelming evidence of its ravages, based on its occurrence, in remote parts of the human organism—the heart, nerves (Leyden), and bones (Ullman), and only to be explained by metastasis; but of very recent date are the clinical observations pointing to its affection of muscles. Such a case came under my care.

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[1] Read before the Genito-urinary Section of the New York Academy of Medicine, April 17, 1901.